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Lectins: Magic Bullet towards HIV gp120

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The AIDS epidemic, in spite of considerable efforts is continues to spread at formidable rate worldwide with an estimated 34 million people being infected with HIV at the end of 2010. Drug discovery towards AIDS is a desperating area of research because of the down beating results of number of painstaking attempts.

The key step in the disease progression is viral binding to the host T lymphocytes and the entry. The gp120 and gp41 glycoproteins, derived from gp160 forms a complex that mediates the receptor and co receptor binding, subsequent membrane fusion events will permit viral entry. These envelope glycoproteins are about 50% glycosylated with N- linked mannose rich glycans [1]. Wei et al. [2] suggests glycan shield concept that the flexible N-linked high mannose glycan buckler prevents the neutralizing antibodies from binding to their cognate epitopes by the steric hindrance rather than the epitope variability.

Lectins are multivalent carbohydrate binding proteins which recognize diverse sugar structures with a high degree of stereospecificity in a non catalytic manner. Number of lectins possess emblemtic attribute of specifically recognize and binds to the carbohydrates/ glycans found on the HIV buckler- envelope glycoprotein. Many lectins found in the human system play key roles in innate immune system against HIV infection. Langerin, a calcium dependent lectin found on mucosal Langerhan's cells bind to HIV-1 and subsequently internalizes it into Birbeck granules which will further get degraded [3]. Mannose binding lectin in human system neutralizes HIV-1 and also blocks the interaction between virus and DC-SIGN, a receptor essential for viral progression [4].

Likely there are wide array of lectins found in natural systems of plants- BanLec from Banana; Algae- Griffithsin from Griffithsia Sp.; Fungi- Pleurotus citrinopileatus lectin from *Pleurotus citrinopileatus*; Actinohivin from Actinomycetes; Cyanobacteria- Cyanovirin V from Nostoc.

It is worth focusing on recent developments in antiretrovirals, as most of the current drug regimns suffer from the events of developing resistance against existing combination of therapies. HIV evades the antibody mediated neutralization in many cunning ways with the help of evolving glycan coat. Initially glycans were thought to be ornaments of envelope in HIV coat. Later they are knew to have vital role in disease initiation and progression. The glycan coat is important for the hindrance and survival from immune system. Glycans on HIV envelope glycoproteins provided by the host machinery, hence chances of acquiring the resistance from altering the glycan structure is very less. Lectins can bind to the glycans found on different spots of the HIV-1 envelope, and presumably it will take multiple mutations for the virus to get around them.

Many studies showed that alteration/removal of carbohydrates in the viral glycan coat make it more susceptible for host immune system [5]. Thus targeting the glycan coat is an effective approach in halting the spread of HIV infection.

Compared with the drugs which are already in the clinical trials ex; Maraviroc, Lectins found to be potent entry blocker of HIV-1 and subsequently inhibit progression and transmission of disease [6]. Apart from the entry/fusion inhibition by binding to gp120, they also serve as Reverse Transcriptase inhibitors [7], Immune potentiators- studied with inducing the expression of IFN-γ, TNF-α and IL-2 in splenocytes8. Lectins also inhibit other microbes- *Klebsiella pneumonia*, HCV, which are common opportunistic infections during AIDS. Thus lectins as a single or in a group may demonstrate synergism thus offering the rationale for their combination in therapies for HIV infection [8].

Many efforts put forth towards the synthesis of highly potent lectins which are more active with poor toxic profile. University of Utah researchers headed by Patrick. F. Kiser have constructed benzoboroxole-based synthetic lectin, inhibits HIV entry into host cells (EC50=1.1 nM) [9]. US based Legere Pharmaceuticals Ltd. developing many lectin based commercial biopharmaceuticals- Phytocam VM (vaginal microbicide), Phytocam condom (utilize single or multiple lectins targeted at HIV) and claimed patents on method of using lectin for prophylaxis against diseases transmittable by sexual contact.

There are many approaches for potentially more promising delivery of lectins, is there *in situ* expression by modified bacteria similar to those naturally found in vagina. This was already proven by studies of the delivery of Cyanovirin V in biologically active form using human commensal organism *Streptococcus gordonii* [10,11]. Altogether these promising profiles provide new insight for antiretroviral research and suggest that lectins will be effective tools, which could serve as microbicides in order to interrupt HIV transmission in humans.

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References

1. Pantophlet R, Burton DR (2006) GP120: target for neutralizing HIV-1 antibodies. Annu Rev Immunol 24: 739-69.
2. Wei X, Decker JM, Wang S, Hui H, Kappes JC, et al. (2003) Antibody neutralization and escape by HIV-1. Nature 422: 307-312.
3. de Witte L, Nabatov A, Pion M, Fluitsma D, de Jong MA, et al. (2007) Langerin is a natural barrier to HIV-1 transmission by Langerhans cells. Nat Med 13: 367-371.
4. Ji X, Gewurz H, Spear GT (2005) Mannose binding lectin (MBL) and HIV. Mol Immunol 42: 145-52.

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5. Koch M, Pancera M, Kwong PD, Kolchinsky P, Grundner C, et al. (2003) Structure-based, targeted deglycosylation of HIV-1 gp120 and effects on neutralization sensitivity and antibody recognition. Virology 313: 387-400.

6. Swanson MD, Winter HC, Goldstein IJ, Markovitz DM (2010) A Lectin Isolated from Bananas Is a Potent Inhibitor of HIV Replication. J Biol Chem 285: 8646-8655.

7. Zhao S, Zhao Y, Li S, Zhao J, Zhang G, et al. (2010) A novel lectin with highly potent antiproliferative and HIV-1 reverse transcriptase inhibitory activities from the edible wild mushroom Russula delica. Glycoconj J 27: 259-265.

8. Cheung AH, Wong JH, Ng TB (2009) Musa acuminata (Del Monte banana) lectin is a fructose-binding lectin with cytokine-inducing activity. Phytomedicine 16: 594-600.

9. Mahalingam A, Geonnotti AR, Balzarini J, Kiser PF (2011) Activity and safety of synthetic lectins. Mol Pharm 8: 2465-75.

10. Mahalingam A, Geonnotti AR, Balzarini J, Kiser PF (2011) Activity and safety of synthetic lectins based on benzoboroxole-functionalized polymers for inhibition of HIV entry. Mol Pharm 8: 2465-2475.

11. Giomarelli B, Provvedi R, Meacci F, Maggi T, Medaglini D, et al. (2002) The microbicide cyanovirin-N expressed in the surface of commensal bacterium Streptococcus gordonii captures HIV-1. AIDS 16: 1351-1360.